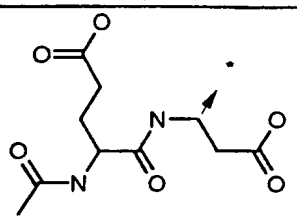
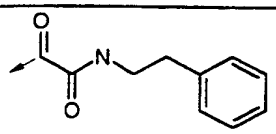
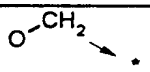
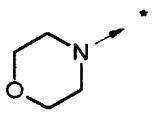
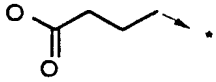
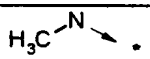
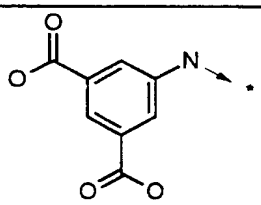
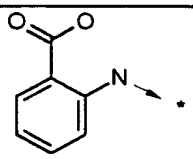
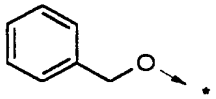
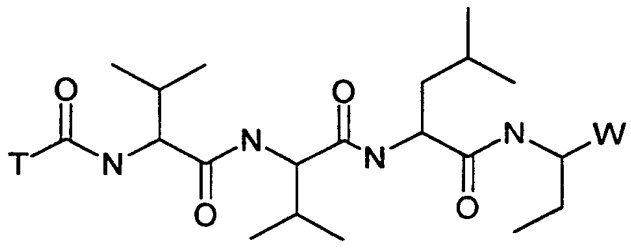
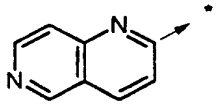
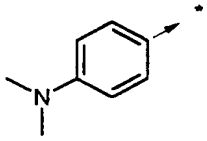
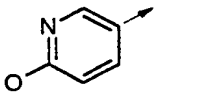
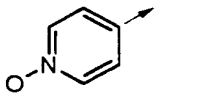
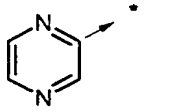
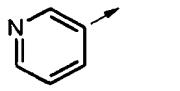
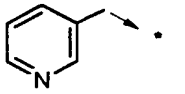
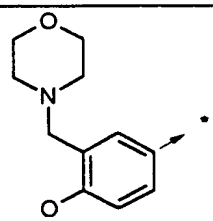
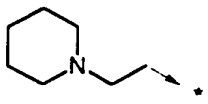
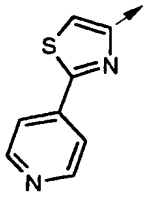
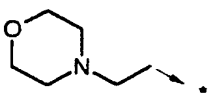
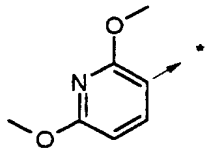
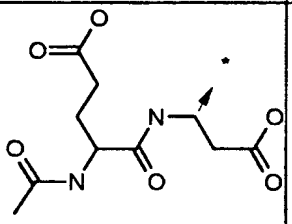
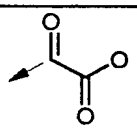
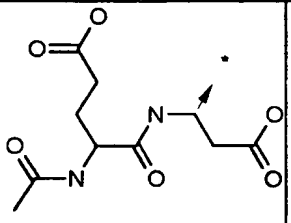
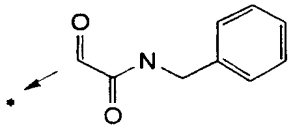
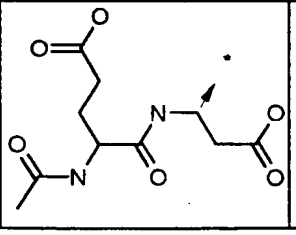
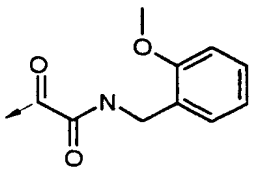
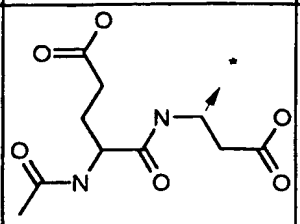
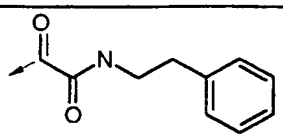
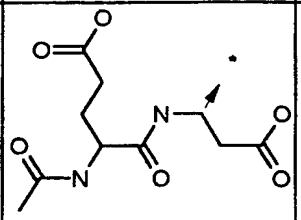
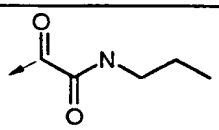
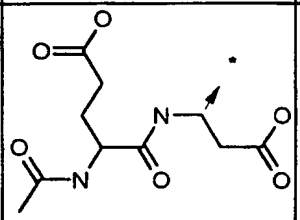
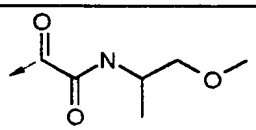
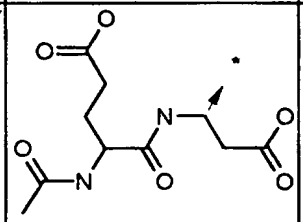
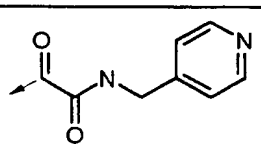
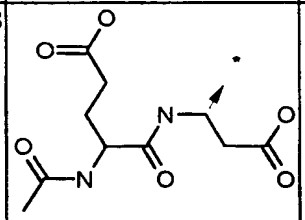
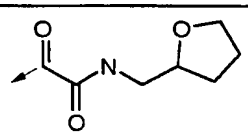
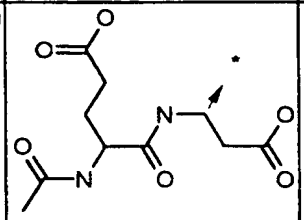
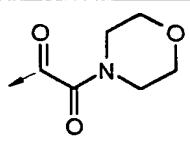
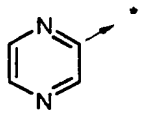
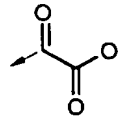
	T	W	MS Data	HPLC
80			(M+H)= 947	20-70%B; 6.15 min.; 95%
81		C(O)H	(M+Na)= 553.60	5-45%B; 11.699 min.; 100%
82		C(O)H	(M+H)= 547.4	5-45%B; 11.083 min.; 100%
83		C(O)H	(M+Na)= 625.3	5-45%B; 12.258 min.; 100%
84		C(O)H	(M+Na)= 626.5	5-45%B; 11.083 min.; 100%
85		C(O)H	(M+Na)= 569.5	5-45%B; 11.606 min.; 100%
86		C(O)H	(M+Na)= 717.2	5-45%B; 7.942 min.; 100%
87		C(O)H	(M+H)= 655.3	15-55%B; 10.735 min.; 100%
88		C(O)H	(M+Na)= 644.1	20-60%B; 11.360 min.; 98%

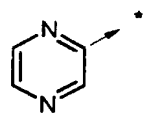
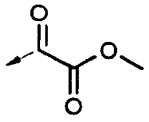
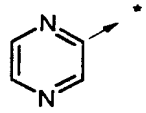
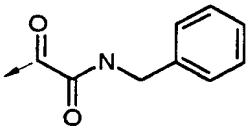
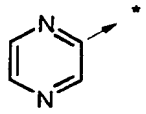
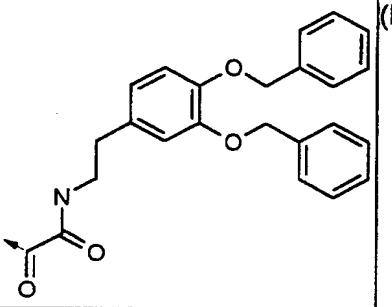
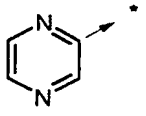
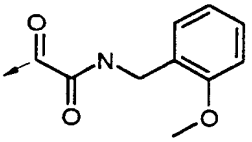
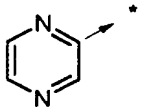
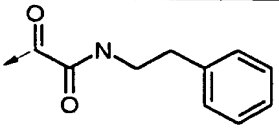
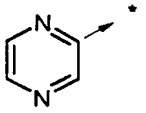
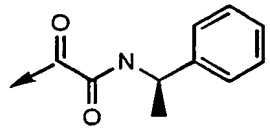
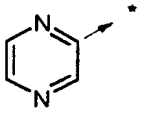
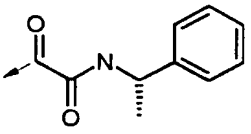
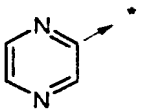
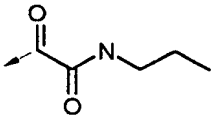
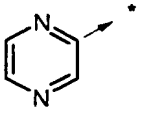
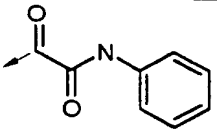
Table 4 Structures and analytical data - compounds 89-126



	T	W	MS Data	HPLC
89		C(O)H	(M+H)= 555.9	5-45% B; 10.771 min.; 99%
90		C(O)H	(M+H)= 556.0	5-45% B; 13.055 min.;95%
91		C(O)H	(M+H)= 522.4	5-45%B; 9.485 min.; 97%
92		C(O)H	(M+H)= 522.55	5-45%B; 9.072 min.; 100%
93		C(O)H	(M+H)= 506.33	5-45%B; 11.775 min.; 97%
94		C(O)H	(M+Na)= 526.6	5-45%B; 8.822 min.; 100%
95		C(O)H	(M+H)= 518.	5-45%B; 8.484 min.; 100%
96		C(O)H	(M+H)= 619.6	5-45%B; 9.944 min.; 90%

	T	W	MS Data	HPLC
97		C(O)H	(M+H)= 538.7	5-45%B; 9.099 min.; 100%
98		C(O)H	(M+H)= 588.6	5-45%B; 10.388 min.; 95%
99		C(O)H	(M+H)= 541.1	5-45%B; 8.326 min.; 100%
100		C(O)H	(M+Na)= 587.3	35-75%B; 6.763 min.; 95%
101			(M+H)= 729	10-80%B; 3.0 min; 95%
102			(M+H)= 819; (M+Na)= 840	20-70%B; 6.9 min; 95%
103			(M+H)=848; (M+Na)= 870	20-70%B; 6.3 min; 95%

	T	W	MS Data	HPLC
104			(M+H)= 833	20-70%B; 7.3 min; 95%
105			(M+H)=770; (M+Na)=792	20-70%B; 6.0 min; 95%
106			(M+H)= 801; (M+Na)= 822	20-70%; 5.9 min; 95%
107			(M+H)=819; (M+Na)= 841	20-70%B; 3.24 min; 95%
108			(M+H)=812; (M+Na)=834	20-70%B; 4.9 min; 95%
109			(M+H)=798; (M+Na)=820	20-70%B; 4.21 min; 95%
110			(M+H)= 550	10-40%B; 7.0 min; 95%

	T	W	MS Data	HPLC
111			(M+Na)= 886	10-50%B; 7.5 min; 95%
112			(M+H)= 638	10-80%B; 6.5 min; 95%
113			(M+H)= 865	40-80%B; 5.7 min; 95%
114			(M+H)= 669; (M+Na)= 693	25-40%B; 11.6 min; 95%
115			(M+H)= 653	10-80%B; 6.80 min; 95%
116			(M+H)= 653	10-80%B; 6.7 min; 95%
117			(M+H)= 653	10-80%B; 6.7 min; 95%
118			(M+Na)= 611	10-80%B; 5.62 min; 95%
119			(M+H)= 624	10-80%B; 12.1 min; 95%

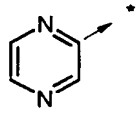
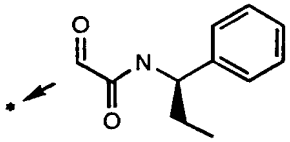
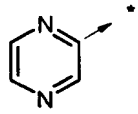
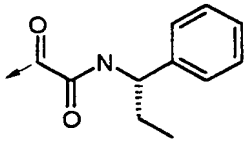
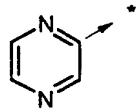
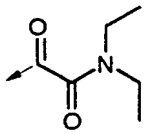
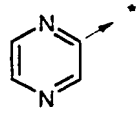
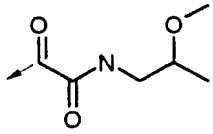
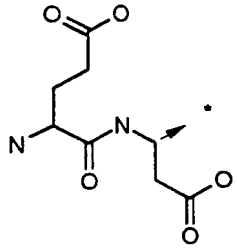
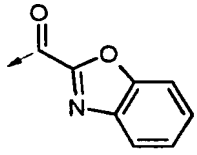
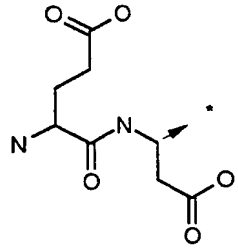
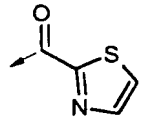
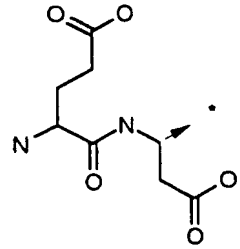
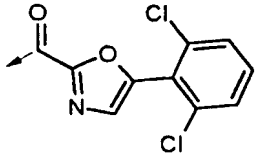
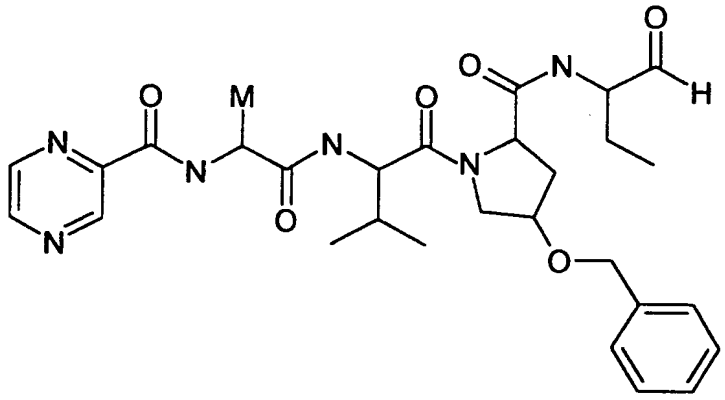
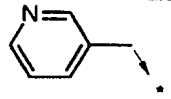
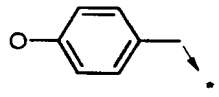
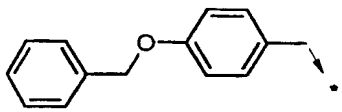
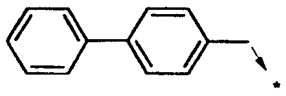
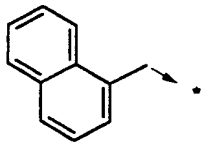
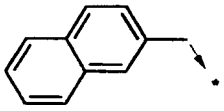
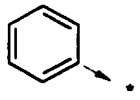
	T	W	MS Data	HPLC
120			(M+H)= 667	10-80%B; 13.4 min; 95%
121			(M+H)= 667	10-80%B; 13.3 min; 95%
122			(M+H)= 605	10-80%B; 11.0 min; 95%
123			(M+H)= 621	10-80%B; 9.7 min; 95%
124			(M+H)= 761	13.65 min.; 90%
125			(M+H)= 727	ND
126			(M+H)= 856	ND

Table 5 Structures and analytical data - compounds 127-142



	M	MS Data	HPLC
127		(M+H)= 644.30	15-55%B; 6.08 min; 100%
128		(M+H)= 681.3	20-60%B; 8.11 min; 100%
129		(M+H)= 750.6	30-70%B; 6.99 min; 100%
130		(M+H)= 720.2	30-70%B; 6.71 min; 100%
131		(M+Na)= 715.4	30-70%B; 5.64 min; 100%
132		(M+Na)= 715.2	30-70%B; 5.58 min; 100%
133		(M+H)= 630.9	30-70%B; 3.78 min; 100%

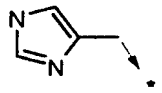
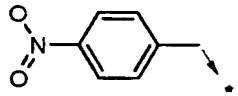
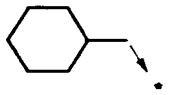
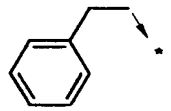
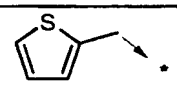
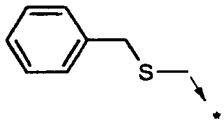
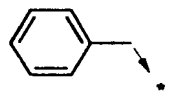
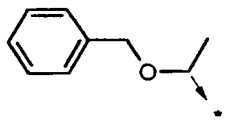
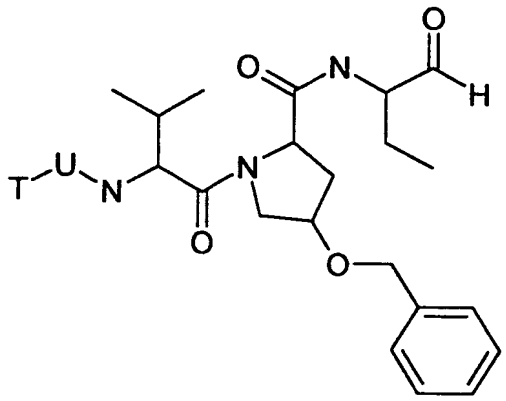
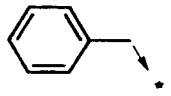
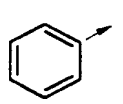
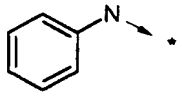
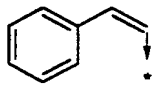
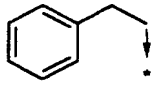
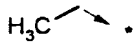
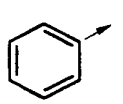
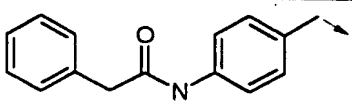
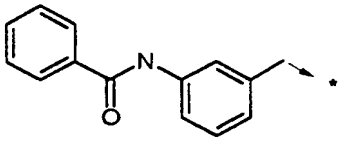
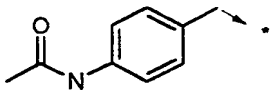
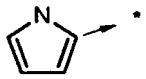
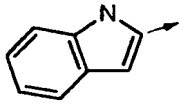
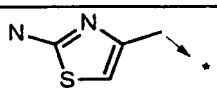
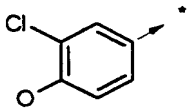
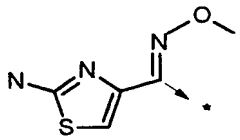
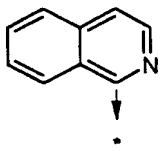
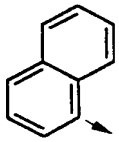
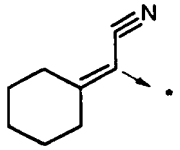
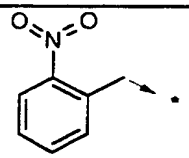
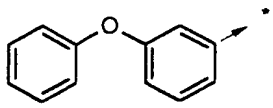
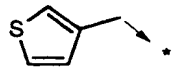
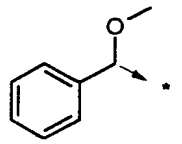
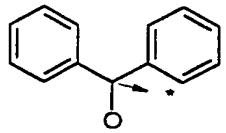
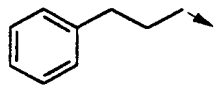
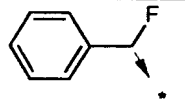
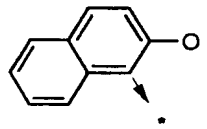
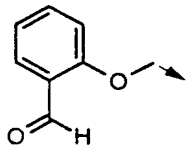
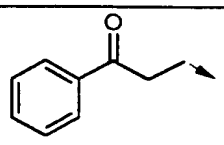
	M	MS Data	HPLC
134		(M+H)= 634.0	15-55%B; 5.90 min; 100%
135		(M+H)= 691.60	30-70%B; 4.22 min; 100%
136		(M+H)= 651.20	40-80%B; 5.59 min; 100%
137		(M+H)= 659.10	40-80%B; 4.65 min; 100%
138		(M+H)= 651.70	40-80%B; 3.83 min; 100%
139		(M+H)= 582.90	40-80%B; 2.34 min; 100%
140		(M+H)= 690.70	40-80%B; 5.15 min; 100%
141		(M+Na)= 664.80	40-80%B; 3.93 min; 100%
142		(M+Na)= 708.80	40-80%B; 5.398 min; 100%

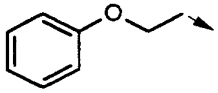
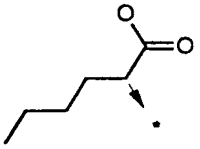
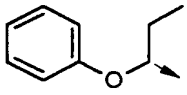
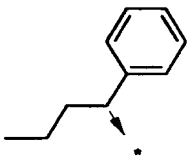
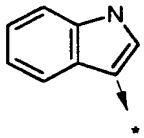
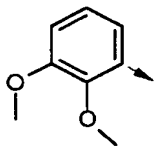
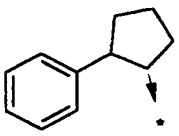
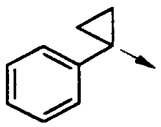
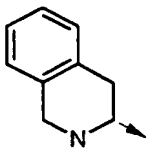
Table 6 Structures and analytical data - compounds 143-197

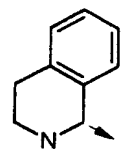
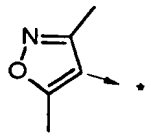
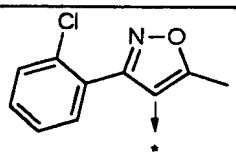
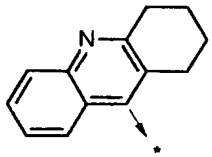
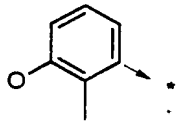
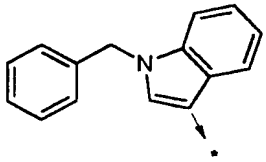
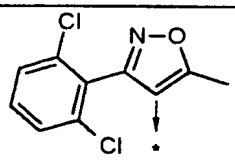
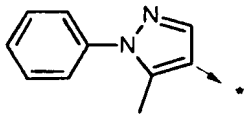
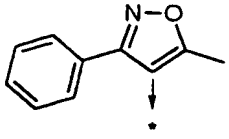


	T	U	MS Data	HPLC
143		$S(O_2)$	(M+Na)= 566.71	20-80%B; 10.186 min.; >95%
144		$S(O_2)$	(M+Na)= 552.26	20-80%B; 9.985 min.; 90%
145		C(O)	(M+Na)= 531.60	20-80%B; 9.978 min; 95%
146		C(O)	(M+Na)= 542.37	20-80%B; 10.404 min; 95%
147		C(O)	(M+Na)= 544.42	20-80%B; 10.246 min; 95%
148		C(O)	(M+Na)= 454.26	20-80%B; 7.109 min; 95%
149		C(O)	(M+Na)= 516.05	20-80%B; 9.668 min; 95%
150		C(O)	(M+Na)= 649.17	20-80%B; 9.880 min; 95%

	T	U	MS Data	HPLC
151		C(O)	(M+Na)= 648.45	20-80%B; 10.030 min; 95%
152		C(O)	(M+Na)= 587.08	20-80%B; 7.892 min; 95%
153		C(O)	(M+Na)= 505.47	20-80%B; 8.583 min; 95%
154		C(O)	(M+Na)= 554.96	20-80%B; 10.411 min; 95%
155		C(O)	(M+Na)= 551.90	20-80%B; 6.737 min; 95%
156		C(O)	(M+Na)= 566.11	20-80%B; 9.227 min; 95%
157		C(O)	(M+Na)= 594.59	20-80% B; 7.567 min; 95%
158		C(O)	(M+Na)= 567.00	20-80%B; 10.409 min; 95%
159		C(O)	(M+Na)= 566.10	20-80%B; 10.716 min; 95%
160		C(O)	(M+Na)= 559.27	20-80%B; 10.597 min; 95%

	T	U	MS Data	HPLC
161		C(O)	(M+Na)= 574.66	20-80%B; 9.723 min; 95%
162		C(O)	(M+Na)= 607.43	20-80%B; 12.019 min; 95%
163		C(O)	(M+H)= 514.83	20-80%B; 6.170 min; 95%
164		C(O)	(M+H)= 538.87	20-80%B; 7.094 min; 99%; 20-80%B; 6.712 min; 99%
165		C(O)	(M+Na)= 620.77	20-80%B; 8.390 min; 99%
166		C(O)	(M+H)= 536.44	20-80%B; 7.787 min; 99%
167		C(O)	(M+H)= 525.58	20-80%B; 7.023 min; 99%
168		C(O)	(M+Na)= 582.25	20-80%B; 7.220 min; 98%
169		C(O)	(M+H)= 552.32	20-80%B; 6.410 min; 99%
170		C(O)	(M+H)= 550.77	20-80%B; 6.663 min; 99%

	T	U	MS Data	HPLC
171		C(O)	(M+H)= 538.87	20-80%B; 7.101 min; 99%
172		C(O)	(M+Na)= 554.79	20-80%B; 7.011 min; 99%
173		C(O)	(M+H)= 551.59	20-80%B; 8.029 min; 96%
174		C(O)	(M+H)= 549.86	20-80%B; 7.320 min; 99%
175		C(O)	(M+Na)= 554.79	20-80%B; 6.413 min; 99%
176		C(O)	(M+H)= 555.05	20-80%B; 7.065 min; 99%
177		C(O)	(M+Na)= 584.55	20-80%B; 9.099 min; 99%
178		C(O)	(M+H)= 535.23	20-80%B; 8.038 min; 99%
179		C(O)	(M+Na)= 569.07	10-80%B; 5.885; 98%

	T	U	MS Data	HPLC
180		C(O)	(M+H)= 548.03	10-80% B; 5.991; 99%
181		C(O)	(M+Na)= 533.91	10-80%B; 7.237; 99%
182		C(O)	(M+Na)= 630.91	10-80%B; 9.382; 95%
183		C(O)	(M+H)= 599.4	10-80% B; 7.0 min; 99%
184		C(O)	(M+Na)= 545.27	10-80%B; 6.89 min; 99%
185		C(O)	(M+Na)= 643.91	10-80%B; 10.43 min; 99%
186		C(O)	(M+Na)= 664.69	10-80%B; 9.95 min; 99%
187		C(O)	(M+Na)= 595.53	10-80%B; 8.61 min; 99%
188		C(O)	(M+Na)= 596.45	10-80%B; 9.0 min; 92%

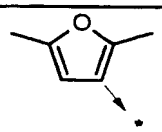
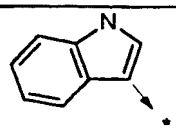
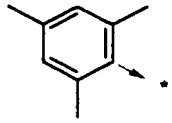
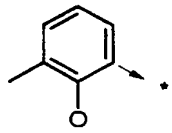
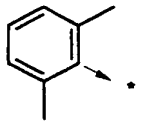
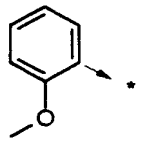
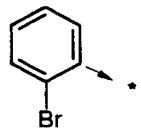
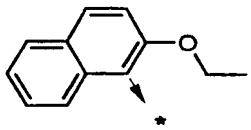
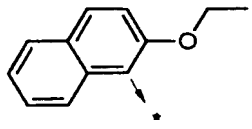
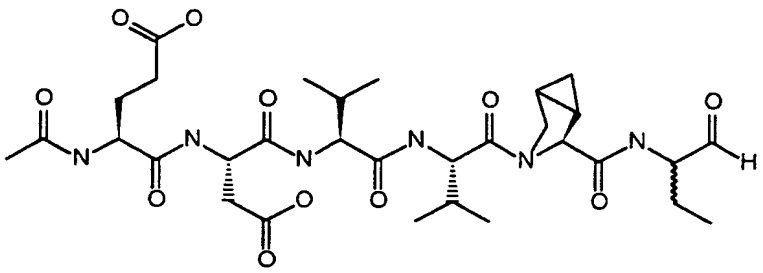
	T	U	MS Data	HPLC
189		C(O)	(M+Na)= 533.73	10-80%B; 8.438; 99%
190		C(O)	(M+Na)= 554.20	10-80%B; 7.990; 99%
191		C(O)	(M+Na)= 557.74	10-80%B; 9.06 min; 99%
192		C(O)	(M+Na)= 545.70	10-80%B; 10.11 min; 99%
193		C(O)	(M+Na)= 544.06	10-80%B; 8.41 min; 99%
194		C(O)	(M+Na)= 545.49	10-80%B; 8.41 min; 96%
195		C(O)	(M+Na)= 594.05	10-80%B; 8.3 min; 99%
196		C(O)	(M+H)= 574.3	10-80%B; 8.84 min; 98%
197		C(O)	(M+H)= 588.4	10-80%B; 9.37 min; 99%

Table 7 Structure and analytical data - compound 198.



	MS Data	HPLC
198	(M+Na)= 702.4	10-60%B; 4.2 min.; >95%

Example 11

Insofar as compounds of formula (I) or (II) are able to inhibit NS3 serine protease, they are of evident clinical utility for the treatment of viral diseases, including HCV. These tests are predictive of the compounds ability to inhibit HCV in vivo.

Peptides and Assays.

Peptides EDVV abuCSMSY (Abu designates - aminobutyric acid), DEMEECSQHLPYI, ECTTPCSGSWLRD and EDVV AbuC-p-nitroanilide was purchased from AnaSpec Inc. (San Jose, CA).

Peptide content of purified, lyophilized peptides and in-house peptides was determined by quantitative nitrogen analysis and the appropriate values were used in preparing stock peptide solutions (Galbreath). pKa determinations were determined by Robertson Microlit Laboratories, Inc. (Madison, NJ).

HPLC cleavage assays were performed using 25 nM to 3.0 µM enzyme in 100 µL volumes at 30 C containing 50 mM HEPES-KOH (pH 7.8), 100 mM NaCl, 20% glycerol, 5 mM DTT and the appropriate amount of substrate (in DMSO),

with or without NS4A peptide, such that the final concentration of DMSO did not exceed 4%. Separate control experiments verified that this percentage of DMSO did not effect enzymatic activity. Cleavage reactions were quenched by the addition of an equal volume of a mixture of 10% TFA: acetonitrile (1:1) and activity was assessed on a reversed phase HPLC column (Rainin C18 Microsorb-MV, 5mm, 4.6 x 250mm; 0-50% acetonitrile, 0.1% TFA @ 3.33% min) using a Hewlett Packard 1050 instrument with auto-injection and diode array detection at 210 nm and 280 nm (where appropriate). Peptide elution fragments were collected and identified by mass spectrometry and N-terminal sequence analysis. Fragment identity and concentration was further verified by authentic, synthesized products. Initial rates of cleaveage were determined at < 20% substrate conversion and catalytic parameters were determined assuming Michaelis-Menten kinetics using the MultiFit program (Day Computing, Cambridge, MA).

Spectrophotometric assays were run in a 96-well microtiter plate at 30 C, using a SpectraMax 250 reader (Molecular Devices, Sunnyvale, CA) with kinetic capability. Cleavage of EDVV AbuC-p-nitroanilide (5A-pNA) substrate was performed with or without NS44 in the same buffer used for HPLC assays at 30 C, and pNA release was monitored at 405 nm. The extinction coefficient of p-nitroaniline is independent of pH at values of 5.5. and above [Tuppy , H., et al., Hoppe-Seyler's Z. Physiol. Chem., 329, pp. 278-288 (1962)]; Raybuck and Luong, unpublished obervations). The percentage of DMSO did not exceed 4% in these assays.

Determination of the pH dependence of Vmax, K_m and V_{max}/K_m was performed using a series of constant ionic strength buffers containing 50 mM MES, 25 Nm Tris, 25 mM ethanolamine and 0.1 M NaCl [Morrison, J.F. and Stone,

R.F., Biochemistry, 27, pp. 5499-5506 (1988)]. The inflection point for log V data was calculated by nonlinear least squares fit of the data to the equation.

$$\log v = \log[V_{max}/(1 + H/K_a)]$$

[Dixon, M. and Webb, E. C. Enzymes; Academic Press: New York; Vol., pp. 138-164 (1979)]. The inflection points for log (V/K) data were calculated by nonlinear least squares fit of the data to the equation

$\log v = \log[V_{max}/(1 + H/K_a + K_b/H)]$ [Dixon, M. and Webb, E. C. Enzymes; Academic Press: New York; Vol., pp. 138-164 (1979)]. The program KineTic (BioKin Ltd) was used in both cases.

Kinetic constants for the rapid equilibrium ordered bisubstrate reaction were determined from rate *vs* [4A], [EDVV AbuC-pNA] data by non-linear least squares fitting to equation 1 [Morrison, J.F. Biochim. Biophys. Acta., 185, pp. 269-286 (1969)] as described in the text. K_{ii} and K_{is} values for peptidyl inhibitors were determined from rate *vs* [inhibitor], [substrate] data and fitting to the equation for mixed inhibition:

$$\text{rate} = V_{max}[S]/\{K_m(1+[I]/K_{is}) + [S]\ (1 + [I]/K_{ii})\}$$

The commercial program KinetAsyst (StateCollege, PA) was used for both procedures. Ki values were calculated from rate *vs* [inhibitor] plots by a nonlinear least squares fit of the data to the equation of Morrison for tight binding competitive inhibition [Morrison, J.F. Biochim. Biophys. Acta., 185, pp. 269-286 (1969)]. The KineTic program (BioKin Ltd) was used for this procedure.

The results are shown in Table 9. K_i values are expressed in μM. Category "A" indicates < 1 μM inhibition; category "B" indicates 1-100 μM inhibition; category "C" indicates > 100 μM. The designation "ND" indicates that the compound was not tested.

Table 9. Enzyme inhibition data for compounds 1-198.

Cmpd. No.	Ki (μM)	Cmpd. No.	Ki (μM)	Cmpd. No.	Ki (μM)
1	B	42	B	83	B
2	B	43	B	84	B
3	B	44	B	85	B
4	B	45	B	86	B
5	B	46	B	87	B
6	B	47	B	88	B
7	B	48	B	89	B
8	B	49	B	90	B
9	B	50	B	91	B
10	B	51	B	92	B
11	B	52	B	93	B
12	B	53	B	94	B
13	B	54	B	95	B
14	B	55	B	96	B
15	B	56	C	97	B
16	B	57	B	98	B
17	B	58	B	99	B
18	B	59	B	100	B
19	B	60	C	101	A
20	B	61	C	102	A
21	B	62	B	103	A
22	B	63	B	104	A
23	B	64	B	105	A
24	B	65	B	106	A
25	B	66	B	107	A
26	B	67	C	108	A
27	B	68	C	109	B
28	B	69	B	110	B
29	B	70	B	111	C
30	B	71	A	112	B
31	B	72	B	113	B
32	B	73	B	114	C
33	C	74	B	115	B
34	B	75	B	116	B
35	B	76	C	117	B
36	C	77	C	118	B
37	B	78	B	119	C
38	B	79	B	120	B
39	B	80	A	121	C
40	B	81	B	122	C
41	B	82	B		

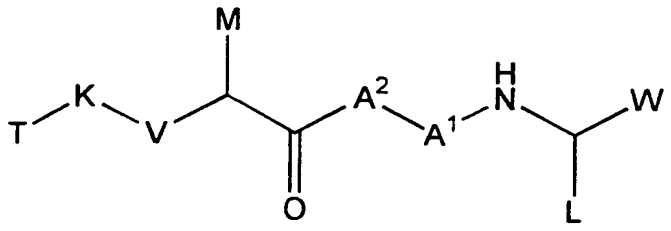
Cmpd. No.	Ki (μM)	Cmpnd. No.	Ki (μM)	Cmpnd No.	Ki (μM)
123	B	149	B	174	B
124	B	150	B	175	B
125	B	151	C	176	C
126	C	152	C	177	C
127	C	153	B	178	C
128	B	154	B	179	B
129	B	155	B	180	C
130	C	156	B	181	C
131	B	157	B	182	C
132	B	158	B	183	B
133	B	159	B	184	B
134	C	160	B	185	B
135	B	161	C	186	C
136	B	162	B	187	C
137	B	163	C	188	C
138	B	164	C	189	C
139	C	165	C	190	C
140	B	166	C	191	C
141	B	167	C	192	C
142	B	168	B	193	C
143	C	169	C	194	C
144	C	170	C	195	B
145	B	171	C	196	B
146	B	172	C	197	B
147	C	173	C	198	A
148	C				

While we have hereinbefore presented a number of embodiments of this invention, it is apparent that my basic construction can be altered to provide other embodiments which utilize the methods of this invention. Therefore, it will be appreciated that the scope of this invention is to be defined by the claims appended hereto rather than the specific embodiments which have been presented hereinbefore by way of example.

CLAIMS

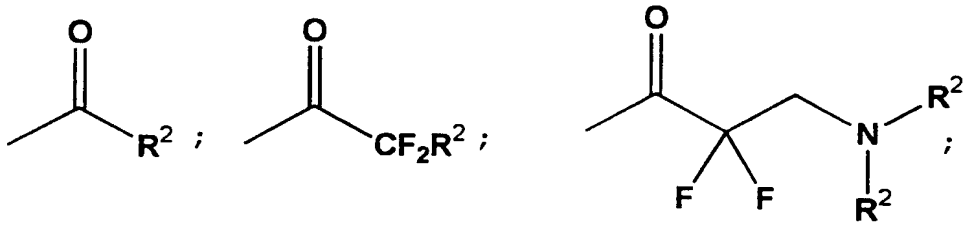
What is claimed is:

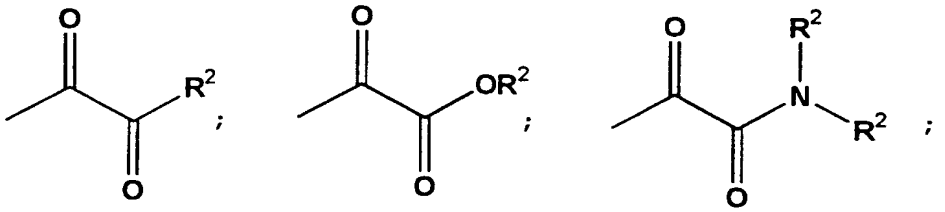
1. A compound of the formula (II):

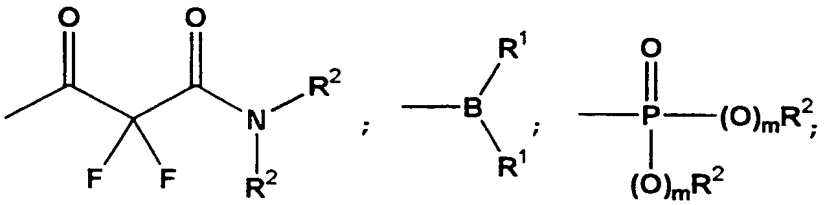
(II) 

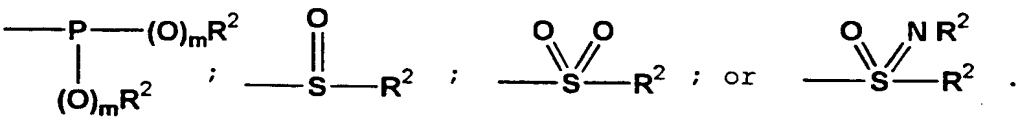
, wherein

W is:









m is 0 or 1;

each R^1 is hydroxy, alkoxy, or aryloxy, or each R^1 is an oxygen atom and together with the boron, to which they are each bound, form a 5-7 membered ring, wherein the ring atoms are carbon, nitrogen, or oxygen;

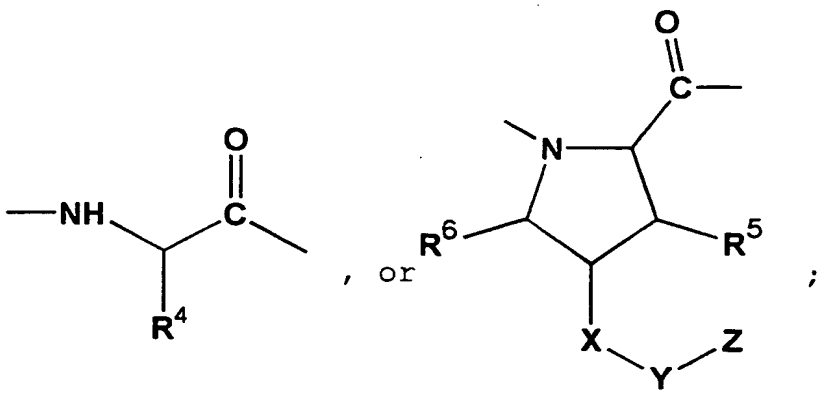
each R^2 is independently hydrogen, alkyl, alkenyl, aryl, aralkyl, aralkenyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heteroaryl, or heteroaralkyl, or two R^2 groups, which are bound to the same nitrogen atom, form together with that nitrogen atom, a 5-7 membered monocyclic heterocyclic ring system; wherein any R^2 carbon atom is optionally substituted with J;

J is alkyl, aryl, aralkyl, alkoxy, aryloxy, aralkoxy, cycloalkyl, cycloalkoxy, heterocyclyl, heterocyclyloxy, heterocyclylalkyl, keto, hydroxy, amino, alkylamino, alkanoylamino, aroylamino, aralkanoylamino, carboxy, carboxyalkyl, carboxamidoalkyl, halo, cyano, nitro, formyl, acyl, sulfonyl, or sulfonamido and is optionally substituted with 1-3 J^1 groups;

J^1 is alkyl, aryl, aralkyl, alkoxy, aryloxy, heterocyclyl, heterocyclyloxy, keto, hydroxy, amino, alkanoylamino, aroylamino, carboxy, carboxyalkyl, carboxamidoalkyl, halo, cyano, nitro, formyl, sulfonyl, or sulfonamido;

L is alkyl, alkenyl, or alkynyl, wherein any hydrogen is optionally substituted with halogen, and wherein any hydrogen or halogen atom bound to any terminal carbon atom is optionally substituted with sulfhydryl or hydroxy;

A^1 is a bond,



R^4 is alkyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroaralkyl, carboxyalkyl, or carboxamidoalkyl, and is optionally substituted with 1-3 J groups;

R^5 and R^6 are independently hydrogen, alkyl, alkenyl, aryl, aralkyl, aralkenyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroaralkyl, and is optionally substituted with 1-3 J groups;

X is a bond, $-C(H)(R^7)-$, $-O-$, $-S-$, or $-N(R^8)-$;

R^7 is hydrogen, alkyl, alkenyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroaralkyl, and is optionally substitituted with 1-3 J groups;

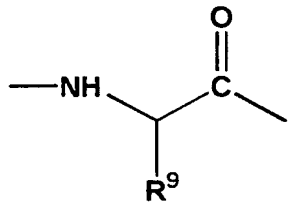
R^8 is hydrogen alkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroaralkyl, aralkanoyl, heterocyclanoyl, heteroaralkanoyl, $-C(O)R^{14}$, $-SO_2R^{14}$, or carboxamido, and is optionally substitituted with 1-3 J groups; or R^8 and Z, together with the atoms to which they are bound, form a nitrogen containing mono- or bicyclic ring system optionally substituted with 1-3 J groups;

R^{14} is alkyl, aryl, aralkyl, heterocyclyl, heterocyclyalkyl, heteroaryl, or heteroaralkyl;

Y is a bond, $-CH_2-$, $-C(O)-$, $-C(O)C(O)-$, $-S(O)-$, $-S(O)_2-$, or $-S(O)(NR^7)-$, wherein R^7 is as defined above;

Z is alkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroaralkyl, $-OR^2$, or $-N(R^2)_2$, wherein any carbon atom is optionally substituted with J, wherein R^2 is as defined above;

A^2 is a bond or



;

R^9 is alkyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroaralkyl, carboxyalkyl, or carboxamidoalkyl, and is optionally substituted with 1-3 J groups;

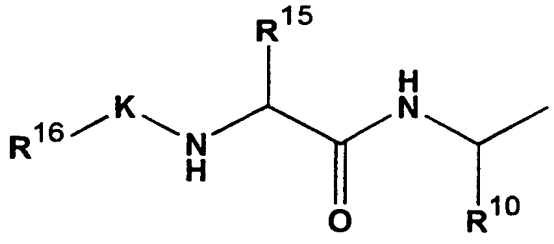
M is alkyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroaralkyl, optionally substituted by 1-3 J groups, wherein any alkyl carbon atom may be replaced by a heteroatom;

V is a bond, $-CH_2-$, $-C(H)(R^{11})-$, $-O-$, $-S-$, or $-N(R^{11})-$;

R^{11} is hydrogen or C_{1-3} alkyl;

K is a bond, $-O-$, $-S-$, $-C(O)-$, $-S(O)-$, $-S(O)_2-$, or $-S(O)(NR^{11})-$, wherein R^{11} is as defined above;

T is $-R^{12}$, -alkyl-R^{12}, -alkenyl-R^{12}, -alkynyl-R^{12}, $-OR^{12}$, $-N(R^{12})_2$, $-C(O)R^{12}$, $-C(=NOalkyl)R^{12}$, or



;

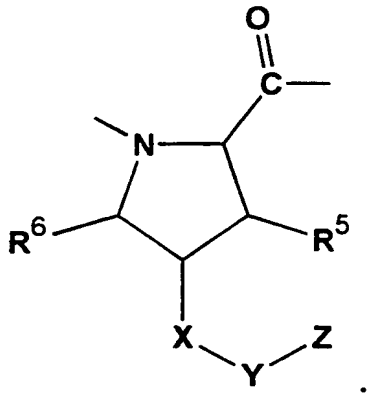
R^{12} is hydrogen, aryl, heteroaryl, cycloalkyl, heterocyclyl, cycloalkylidenyl, or heterocycloalkylidenyl, and is optionally substituted with 1-3 J groups, or a first R^{12} and a second R^{12}, together with the nitrogen to which they are bound, form a mono- or bicyclic ring system optionally substituted by 1-3 J groups;

R^{10} is alkyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroaralkyl, carboxyalkyl, or carboxamidoalkyl, and is optionally substituted with 1-3 hydrogens J groups;

R^{15} is alkyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroaralkyl, carboxyalkyl, or carboxamidoalkyl, and is optionally substituted with 1-3 J groups; and

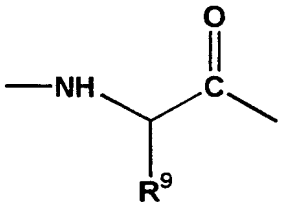
R^{16} is hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, or heterocyclyl.

2. The compound according to claim 1, wherein A1 is:



3. The compound according to claim 2, wherein R^5 and R^6 are hydrogen.

4. The compound according to claim 3, wherein A^2 is:



and R^9 is alkyl.

5. The compound according to claim 4, wherein R^9 is isopropyl.

6. The compound according to claim 5, wherein L is alkyl, alkenyl, or alkynyl, wherein any hydrogen is optionally substituted with halogen, and wherein any hydrogen or halogen atom bound to any terminal carbon atom is optionally substituted with sulfhydryl or hydroxy.

7. The compound according to claim 6, wherein L is trihalomethyl, sulfhydryl, or alkyl substituted with trihalomethyl, sulfhydryl, or hydroxy.

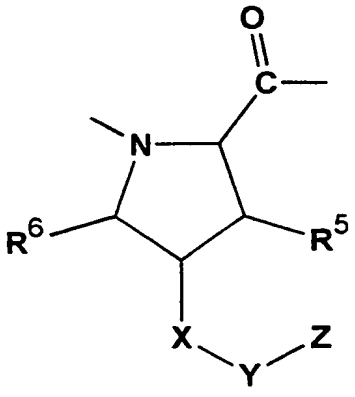
8. The compound according to claim 7, wherein:

X is -O- or -N(H)-; and

Y is $-CH_2-$, -C(O)-, or $-S(O)_2-$.

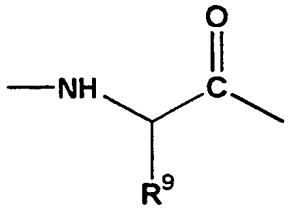
9. The compound according to claim 8, wherein V is -N(H)- and K is -C(O)- or $-S(O)_2-$.

10. The compound according to claim 1, wherein A^1 is:



, and R^5 and R^6 are hydrogen;

A^2 is:



and R^9 is isopropyl;

L is ethyl;

X is -O- or -N(H)-;

Y is $-CH_2-$, -C(O)-, or $-S(O)_2-$;

V is -N(H)-; and

K is -C(O)-.

11. The compound according to claim 10, wherein M is isopropyl.

12. The compound according to claim 11, wherein Z is aryl or heteroaryl.

13. The compound according to claim 12, wherein T is aryl or heteroaryl.

14. The compound according to claim 13, wherein T is pyrazine.

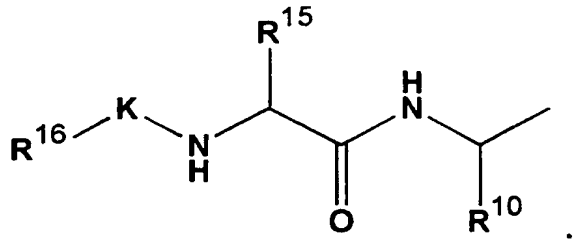
15. The compound according to claim 10, wherein X is -O- and Y is $-CH_2-$.

16. The compound according to claim 15, wherein Z is aryl or heteroaryl.

17. The compound according to claim 16, wherein Z is aryl.

18. The compound according to claim 10, wherein M is isopropyl.

19. The compound according to claim 18, wherein T is $-R^{12}$, $-OR^{12}$, $-N(R^{12})_2$, or



20. The compound according to claim 19, wherein M is alkyl, heteroaralkyl, aryl, cycloalkylalkyl, aralkyl, or aralkyl, wherein one of the alkyl carbon atoms is replaced by O or S.

21. The compound according to claim 20, wherein said heteroatom is S or O.

22. The compound according to claim 21, wherein T is aryl or heteroaryl.

23. The compound according to claim 22, wherein T is pyrazine.

24. The compound according to claim 3, wherein

A^2 is a bond;

L is ethyl;

X is -O-;

Y is $-CH_2-$;

V is -N(H)-; and

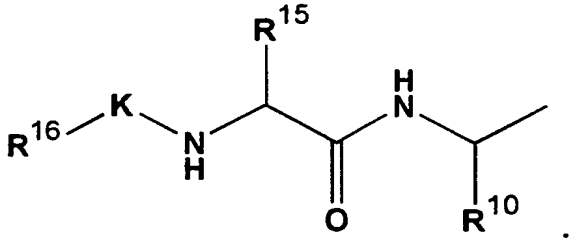
K is $-C(O)-$ or $-S(O)_2-$.

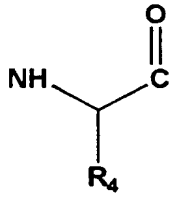
25. The compound according to claim 24, wherein M is isopropyl.

26. The compound according to claim 25, wherein Z is aryl or heteroaryl.

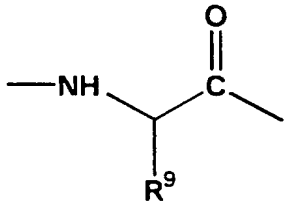
27. The compound according to claim 26, wherein Z is phenyl.

28. The compound according to claim 27, wherein T is $-R^{12}$, $-alkyl-R^{12}$, $-alkenyl-R^{12}$, $-OR^{12}$, $-N(R^{12})_2$, $-C(=NOalkyl)R^{12}$, or



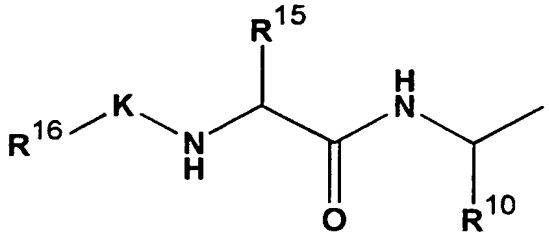
29. The compound according to claim 1, wherein A^1 is  ; and

A^2 is

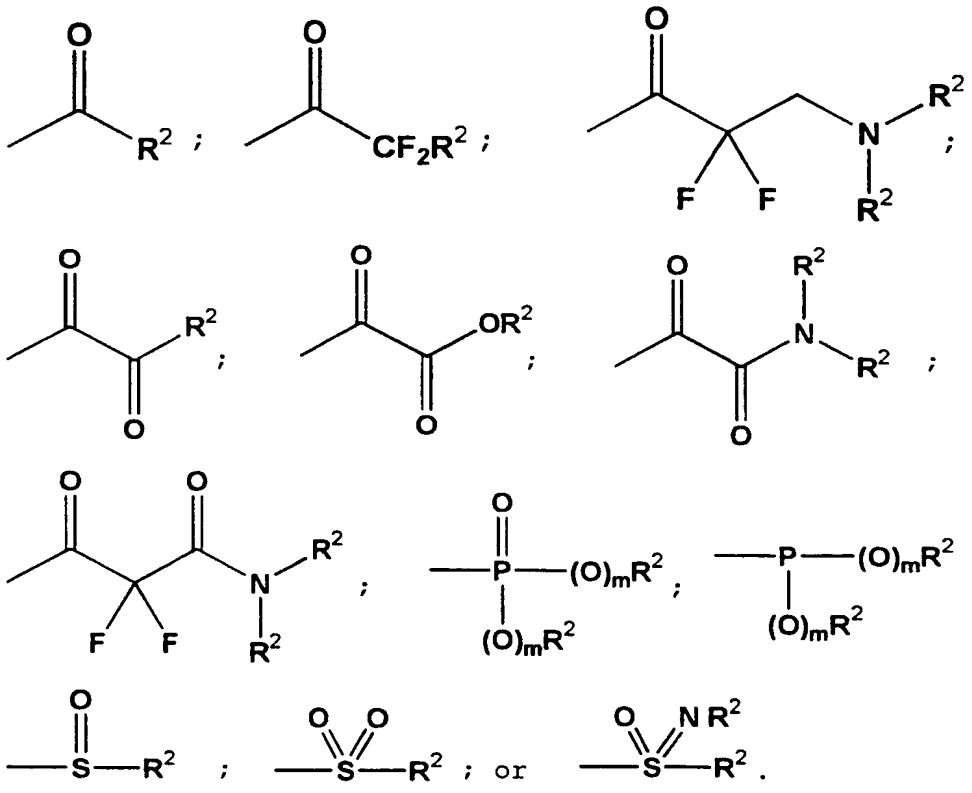


30. The compound according to claim 29, wherein M is isopropyl and K is -C(O)-.

31. The compound according to claim 30, wherein T is $-R^{12}$, -alkyl-R^{12}, -alkenyl-R^{12}, $-OR^{12}$, $-N(R^{12})_2$, $-C(=NOalkyl)R^{12}$, or



32. The compound according to any one of claims 1-31, wherein W is



33. A pharmaceutically acceptable composition comprising:

a) a compound according to claims 1-32 in an amount effective to inhibit HCV NS3 protease; and

b) a pharmaceutically suitable carrier.

34. A method for inhibiting serine protease activity comprising the step of administering to said patient a compound according to any one of claims 1-32.

35. The method according to claim 34, wherein the serine protease is HCV NS3 protease.

36. A method for treating or preventing a hepatitis C viral infection in a patient comprising the step of administering to said patient/mammal a compound according to any one of claims 1-32.

37. The method according to claim 36, wherein said compound is administered to a patient and is formulated together with a pharmaceutically suitable carrier into a pharmaceutically acceptable composition.

INTERNATIONAL SEARCH REPORT

Inte ional Application No
PCT/US 97/18968

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07K5/10 C07K7/06 C07K7/02 C07K5/02 A61K38/55

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95 35308 A (VERTEX) 28 December 1995 see the whole document ---	1-37
A	WO 93 25574 A (PFIZER) 23 December 1993 see the whole document ---	1-37
X	EP 0 363 284 A (MERRELL DOW) 11 April 1990 see the whole document ---	1-37
X	EP 0 195 212 A (MERRELL DOW) 24 September 1986 see the whole document ---	1-37
	-/--	

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

1

Date of the actual completion of the international search	Date of mailing of the international search report
11 March 1998	26. 03. 1998

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Masturzo, P

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Inte ional Application No
PCT/US 97/18968

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	S MEHDI ET AL.: "The inhibition of human neutrophil elastase and cathepsin C by peptidyl 1,2-dicarbonyl derivatives" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS., vol. 166, no. 2, 30 January 1990, ORLANDO, FL US, pages 595-600, XP000085857 see the whole document ---	1-37

1

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 97/18968

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Remark : Although claims 34-37 are directed to a method of treatment of the human/animal body , the search has been carried out and based on the alleged effects of the compound/composition.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int. ional Application No
PCT/US 97/18968

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9535308 A	28-12-95	US 5656627 A	12-08-97
		AU 2944695 A	15-01-96
		BG 101130 A	29-08-97
		CA 2192089 A	28-12-95
		CZ 9603698 A	11-06-97
		EP 0784628 A	23-07-97
		FI 965036 A	14-02-97
		HU 76622 A	28-10-97
		NO 965365 A	17-02-97
		PL 318220 A	26-05-97
		SK 160996 A	10-09-97
		US 5716929 A	10-02-98
WO 9325574 A	23-12-93	CA 2137832 A	23-12-93
		EP 0644892 A	29-03-95
		JP 2668003 B	27-10-97
		JP 7507069 T	03-08-95
EP 363284 A	11-04-90	AT 153029 T	15-05-97
		AU 617875 B	05-12-91
		AU 4249189 A	28-06-90
		AU 626918 B	13-08-92
		AU 4262589 A	12-04-90
		CA 2000340 A	07-04-90
		CA 2000342 A	07-04-90
		CN 1041950 A	09-05-90
		CN 1041951 A	09-05-90
		DE 68928042 D	19-06-97
		DE 68928042 T	28-08-97
		DK 494689 A	08-04-90
		DK 494789 A	08-04-90
		EP 0364344 A	18-04-90
		JP 2256654 A	17-10-90
		JP 2134398 A	23-05-90
		PT 91926 B	03-07-95
		PT 91927 B	03-07-95
EP 195212 A	24-09-86	AU 600226 B	09-08-90
		AU 5288186 A	07-08-86
		DE 3689314 D	05-01-94

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inte ional Application No
PCT/US 97/18968

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 195212 A		DE 3689314 T	19-05-94
		DK 51586 A	05-08-86
		FI 94254 B	28-04-95
		FI 94254 C	10-08-95
		IE 60582 B	27-07-94
		JP 2529825 B	04-09-96
		JP 61183253 A	15-08-86
		US 5496927 A	05-03-96